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Rasmussen's encephalitis: Experience from a developing country based on a group of medically and surgically treated patients

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ABSTRACT

Purpose: To describe the attributes of patients with Rasmussen's encephalitis (RE) seen in a tertiary epilepsy referral center in southern India and to enquire factors helpful in predicting responsiveness to immunotherapy.

Methods: We diagnosed RE based on the European consensus criteria. To assess the factors that could potentially predict the natural course and therapeutic outcome, we subcategorized our patients according to age at onset (</> 6 years), duration from onset to presentation (</> 2 years), immunotherapy versus surgery, and early (≤2 years from the onset) versus late surgery.

Results: The median age at disease onset of 19 patients was 6.0 years (range 2.3–13 years). Epilepsia partialis continua (EPC) and hemiparesis were noted in 14 (73.6%) and 16 (84.2%) patients, respectively. One patient, who presented with dysarthria due to tongue EPC, did not have hemiparesis despite having had the disease for over 15 years. The MRI findings in majority conformed to stage 3 of Bien classification. While 9/10 patients treated by surgery achieved seizure-freedom, only 1/11 patients who received immunotherapy did so. One patient expired due to subsequent development of contralateral hemispheric disease following successful hemispherectomy. None of the factors such as age at onset, age at presentation, presence/absence of antecedents, seizure burden, MRI stage predicted responsiveness to immunotherapy.

Conclusion: This study from a developing country, in addition to substantiating the well known characteristics of RE, noted the following unusual findings: isolated lingual EPC abolished by focal cortical resection, bilateral RE, putaminal atrophy and absence of hemiparesis despite long standing disease.

1. Introduction

Rasmussen's encephalitis (RE) is a devastating disease characterized by progressive unihemispheric affection resulting in medically refractory focal seizures and contralateral neurological deficits.[1,2] RE affects predominantly healthy children and progresses variably through a prodromal phase (with low seizure frequency and mild or no hemiparesis), acute phase (with epilepsia partialis continua and deteriorating limb weakness) and a residual burnt-out phase (stable state with fixed hemiparesis and reduced seizure frequency).[3] Although RE is usually a strictly unihemispheric disease, there have been very rare occurrences of bilateral disease.[4] The European consensus statement on the pathogenesis, diagnosis and treatment has recently proposed a diagnostic criterion that has facilitated the diagnosis of RE (Table 1).[5] Typical cases with characteristic clinical, electrographic and radiological features pose no diagnostic challenges and histopathological or immunological studies are not routinely required to confirm the diagnosis of RE.[5] However, diagnostic difficulties may arise with atypical presentations especially very early into the illness.

The etiopathogenesis of RE is uncertain, although immune mediated mechanisms are implicated.[2,5] The nonspecific nature of antibodies to glutamate receptor GluR3 which was initially proposed to be associated with RE[6] and the recent identification of antibodies to α-7-acetylcholine receptor in patients with biopsy proven RE[7] suggests that the syndrome of RE may encompass several different autoimmune entities.[8] With the description of more and more patients with RE, the high variability in the clinical course and neurological manifestations are becoming increasingly apparent.[3,5]

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Table 1
European consensus diagnostic criteria for Rasmussen's encephalitis (RE).

Part A	
(1) Clinical	Focal seizures with or without EPC and unilateral cortical deficits
(2) EEG	Unihemispheric slowing with or without IEDs and ictal onset
(3) MRI	Unihemisheric focal cortical atrophy plus at least one of following: Grey or white matter T2/FLAIR hyperintense signal Hyperintense signal or atrophy of ipsilateral caudate head
Part B	
(1) Clinical	EPC or progressive unilateral focal cortical deficits
(2) MRI	Progressive unihemispheric focal cortical atrophy
(3) Histopathology	T cell dominated encephalitis with activated microglial cells and reactive astrogliosis. Numerous parenchymal macrophages, B cells or plasma cells or viral inclusion bodies exclude the diagnosis of RE

Note: RE can be diagnosed if either all three criteria of Part A or two out of three criteria of Part B are present. Adapted from Bien et al.[5] EPC—epilepsia partialis continua; IEDs—interictal epileptiform abnormalities.

The seizures in RE are medically refractory and hemispherectomy (variable anatomical resection of the involved hemisphere) or hemispherotomy (unihemispheric disconnection) is often required for seizure control.[2,5] However, surgery is indicated only in patients with contralateral motor deficit and no useful hand function. In patients unsuitable for surgery, immunotherapy with corticosteroids, intravenous immunoglobulins or plasma exchange is an initial alternative option.[5,9,10] RE is very rare and major epilepsy centers across the world do not encounter more than a couple of cases annually.[11] To the best of our knowledge, case series with sizeable number of patients with RE has not been reported from developing countries.

From a tertiary epilepsy center situated in southern India, we report our experience with RE in 19 patients diagnosed over a span of 11 years to address the following two questions: (1) are there any demographical, clinical, electrophysiological, pathological and imaging features that are peculiar to RE seen in this geographical region? and (2) are there any factors that are helpful in predicting the likelihood of patients' responsiveness to immunotherapy vis-à-vis need for early surgical intervention?

2. Patients and methods

Utilizing a structured proforma, we abstracted the clinical, investigative, therapeutic and follow-up data of patients diagnosed with RE from January 1996 to March 2007 from the elaborate prospective data base maintained at the R. Madhavan Nayar Center for Comprehensive Epilepsy Care, Sree Chitra Tirunal Institute for Medical sciences and Technology, Trivandrum, Kerala, southern India. Diagnosis of RE was based on the diagnostic criteria recommended by the European Consensus Statement (Table 1).[5] Patients' demographic profile, birth history, perinatal insults, antecedent illnesses, age at onset of seizures, age at presentation, types of seizures, presence of epilepsia partialis continua (EPC, defined as regular or irregular clonic twitches affecting a limited part of the body lasting $\geq$1 h and recurring at intervals of $<$10 s),[12] history of generalized convulsive status epilepticus, clinical findings on examination during initial presentation and subsequent follow-ups, age at onset of hemiparesis, electroencephalographic and radiological features, progression of the disease, treatment given and outcome were abstracted. In addition to routine scalp electroencephalogram (EEG), prolonged video-EEG monitoring was carried out in 17 patients. EEG data were reviewed by two experienced epileptologists associated with the study (RA and KR). A neuroradiologist experienced in epilepsy neuroimaging and associated with the present study (CK) reviewed the MRI data of all patients performed on a 1.5T scanner (Signa GE, Milwaukee, USA). We staged the MRI abnormalities as proposed by Bien et al.[13] as follows: stage 0—no abnormality, stage 1—hyperintense signal and swelling, stage 2—hyperintense signal and normal brain volume, stage 3—hyperintense signal and atrophy, stage 4—normal signal and progression of atrophy. Treatment decisions were taken after discussing each case at the institutional epilepsy patient management conference. Immunotherapy was considered in patients having no or minimal neurological deficits with reasonably preserved distal upper extremity functions, in patients very early into the illness with nondisabling seizures and those who declined surgical therapy. Immunotherapy consisted of intravenous immunoglobulin (IVIG) at a dosage of at least 2 g/kg over 5 days or intravenous methyl prednisolone at a dosage of 20–30 mg/day for at least 5 days followed by oral steroids for a variable period of 12–24 weeks depending on the response, or both IVIG and steroids. Surgery was offered in patients with medically refractory seizures and contralateral hemiparesis with poor hand function. Either a hemispherotomy which was the procedure of choice in patients with cerebral atrophy or a hemispherectomy when there was no atrophy of brain in which disconnection alone becomes technically demanding was performed. In our center, the technique of functional hemispherectomy includes a radical temporal lobectomy and centro-parietal excision followed by total callosotomy and then frontal and occipital disconnection. One of our patients with EPC of tongue alone without any other deficits, who underwent a limited resection of the fronto-opercular cortex, has already been published.[14] Histopathological examination of the tissues obtained during surgery was undertaken by an experienced neuropathologist associated with the study (VVR). Patients under medical follow-up were regularly followed up every 3 months after treatment, and those who underwent surgery were followed up at 3 months and at 12 months and yearly thereafter. We classified the seizure outcome following immunotherapy and surgery as seizure-free, and in those with continuing seizures as percentage reduction in seizure frequency compared to pre-treatment period and no change. The patients were also assessed for their motor deficit, cognitive capabilities, schooling and employment.

2.1. Statistical analysis

We summarized the quantitative data as percentages, median, range and mean $\pm$ standard deviation (SD). Fisher's exact test was used for categorical variables and Mann–Whitney test for continuous variables for subgroup comparisons. A p value $\leq$0.05 was considered as significant.

3. Results

3.1. Demographic and clinical features

The demographic and clinical characteristics of our 19 patients (12 males, 7 females) with RE are summarized in Table 2 and are individualized in Table 3. The median age at disease onset was 6.0 years (range 2.3–13 years), while the median age at presentation to us was 9 years (range 2.7–22 years). All patients were normal neurologically prior to the onset of seizures. Antecedent events were reported in seven children 1–2 weeks prior to the onset of the seizures (febrile illness in four, vomiting and abdominal pain in two and fall with insignificant head trauma in one). None had family history of seizures. Seizures were the manifesting symptom in all patients. Simple partial seizures (SPS) occurred in all, 16 (84.2%), in addition had complex partial seizures (CPS). Eight patients (42.1%) had history of recurrent generalized status epilepticus necessitating frequent hospitalizations. EPC was noted in 14 (73.6%) patients. In

Table 2
Characteristics of 19 patients with Rasmussen's encephalitis.

Gender (male:female)	12:7
Age at onset (year)	Mean 6.0 ± 2.8 (range 2.3–13.0)
Age at presentation (year)	Mean 10.2 ± 5.5 (range 2.7–22)
Hemisphere involved (right:left)	10:9
	n (%)
Seizure types	
Epilepsia partilis continua	14 (73.6)
Simple partial seizures	19 (100)
Complex partial seizures	16 (84.2)
Generalized tonic/clonic seizures	9 (47.3)
Recurrent convulsive status epilepticus	8 (42.1)
Neurological deficit at presentation	
Hemiparesis	16 (84.2)
Dysphasia	12 (63.2)
Hemianopia (*n* = 6)	6 (100)
Dysarthria	2 (10.5)
Interictal epileptiform EEG discharges	
Ipsilateral	16 (84.2)
Contralateral	3 (15.7)
Ictal EEG onset (*n* = 17)	
Lateralizing	15 (88.2)
Contralateral	2 (11.7)

one of them, EPC predominantly involved side of the tongue contralateral to hemispheric involvement. Hemiparesis of different grades was observed in 16 (84.2%) patients. Hemiparesis occurred after a mean duration of 17.8 months (range 7–22 months) from the onset of seizures. Three patients had no neurological deficits (Patients 8, 11, and 13, Table 3). None had ataxia, dystonia, chorea, rigidity or other extrapyramidal symptoms or signs. Homonymous hemianopia was noted in six patients in whom visual fields could reliably be tested. Out of the 10 patients in whom sensory testing could reliably be performed, two had hemihypestesia on the hemiparetic side. A detailed neuropsychological assessment was possible in only 12 children; they showed variable degree of cognitive impairment. Out of the four patients aged >12 years, one had a subnormal IQ of 50 (Patient 2, Table 3). Expressive and receptive language dysfunction was noted in 12 (63.2%) patients, three with right hemispheric involvement and nine with left hemispheric involvement. In the three patients with right hemispheric disease (Patients 2, 4 and 6, Table 3), the language involvement was considered to be a part of the global cognitive dysfunction they had. All our patients were right handed prior to the onset of the disease. Two patients had dysarthria, one of them due to tongue EPCs (Patient 11, Table 3).

3.2. Electrophysiological data

Interictal epileptiform discharges (IEDs) were noted on the side of hemispheric involvement in 16 patients (84.2%), but were seen only over the contralateral hemisphere in three (15.7%). Interictally, unihemispheric background slowing was seen in 15 patients. Prolonged video-EEG monitoring done in 17 (89.4%) patients recorded seizures arising from the affected hemisphere (lateralizing) in 15 and false lateralized to the unaffected hemisphere in two (Table 2).

3.3. Neuroimaging findings

The MRI findings of our patients are summarized in Table 4. The interval from seizure onset to initial MRI ranged 1–80 months (median 15 months). All had more than one MRI done at varying intervals. Part of our radiological data has already been published.[15] The insular and perisylvian cortex were maximally atrophic in all (Fig. 1). Basal ganglia were affected in all, except one patient (94.7%). Caudate was atrophic in 17 patients (89.4%) while additional putaminal atrophy was seen in 15 (78.9%) patients (Fig. 1). One patient had atrophy involving the globus pallidus as well. Prominent hyperintense signal changes on T2WI or fluid attenuated inversion recovery (FLAIR) sequences were noted in seven patients (36.8%) (Fig. 1). Atrophy of cerebral peduncle and brainstem ipsilateral to the affected hemisphere was noted in 11 patients (57.8%). None of our patients had occipital involvement radiologically. A majority of our patients belonged to stage 3 (15 patients, 78.9%) or stage 4 (three patients, 15.7%) of Bien classification.[13] Gadolinium enhancement was observed in none. Serial imaging revealed progressive hemispheric atrophy 16 (84.2%) patients.

3.4. Treatment and outcome

Despite use of multiple AEDs (mean number of AEDs per patient 4.6, range 2–7), seizure control was poor in all. Immunotherapy was attempted in 11 patients and surgery was undertaken in 10 patients. The outcomes of medically and surgically treated patients are provided in Table 3.

3.4.1. Immunotherapy

Seven of 11 patients received intravenous methyl prednisolone followed by oral steroids; two of them received IVIG prior to steroid treatment. Two patients received IVIG alone. Two patients had no benefit (Patients 12 and 19, Table 3). Nine patients had variable benefits—one patient was seizure-free for 2 years with subsequent relapse (Patient 7, Table 3). This patient had improvement in hemiparesis as well. Four patients were operated subsequently due to refractory disabling seizures. Two patients had daily seizures but were not operated as there was no hemiparesis (Patients 8 and 13, Table 3).

3.4.2. Surgery

Ten patients underwent either hemispherotomy (*n* = 6), hemispherectomy (*n* = 3) or focal resection (*n* = 1). Histopathological examination of the brain tissue showed variable degree of perivascular lymphomononuclear aggregation, microglial nodules and glosis (Fig. 1). During the mean follow-up duration of 2.7 (range 1–10) years, all of them had Engel class I outcome[16] at last follow-up, except one who had seizure recurrence originating from the left hemisphere 2 years after right hemispherectomy with evidence of bilateral disease and succumbed to it (Patient 9, Table 3). Seven of them were seizure-free and aura-free during the whole post-surgery follow-up period (Table 3). Out of nine patients with left hemispheric disease and preoperative language dysfunction, three underwent surgery (Patients 3, 5 and 10, Table 3). Their expressive and receptive language abilities showed a steady improvement during the follow-up period. One patient with tongue EPC and marked dysarthria regained normal articulation after limited resection of frontal opercular region (Patient 11, Table 3).[14] Despite the absence of hemiparesis, severely disabling dysarthria due to lingual EPC prompted this patient to consent for this focal resection after fully understanding its uncertain long-term benefit. This patient continues to be free of lingual EPC and dysarthria when seen recently 3 years after surgery. All except one patient (Patient 2, Table 3), was ambulant at last follow-up, either independently or with minimum support.

3.5. Predictors of outcome

We grouped patients into four categories for comparison, which could potentially predict the natural course of RE and outcome:

Table 3
Clinical profile, treatment and outcome of individual patients with Rasmussen's encephalitis.

No.	Sex/age at presentation	Age at onset (year)	Hemisphere involved	Neurological deficit	Treatment		Duration of follow-up (months)	Outcome at last follow-up
					Immunotherapy	Surgery		
1	M/9	5	Right	Hemiparesis, normal language	MP	–	120	50% reduction in seizures for 3 months
2	F/16	7.5	Right	Hemiparesis, global cognitive and language impairment	–	Hemispherectomy	72	Rare nondisabling seizures, mild improvement in cognition and language, in wheel chair, on one AED
3	F/8	6.5	Left	Mild hemiparesis, dysphasia	IG	Hemispherectomy	48	Seizure-free, nearly normal language function, in regular school, off AED
4	M/16	7	Right	Hemiparesis, global cognitive and language impairment	–	Hemispherotomy	36	Seizure-free, improved language, in special school, on one AED
5	M/11	2.5	Left	Hemiparesis, dysphasia	–	Hemispherotomy	36	Seizure-free improved language, in regular school
6	F/4	3.4	Right	Hemiparesis, global cognitive and language impairment	IG + MP	Hemispherotomy	36	Rare nondisabling seizures, improved language, in special school, on one AED
7	F/6	3.5	Left	Hemiparesis, dysarthria	MP	–	36	Seizure-free for 2 years, hemiparesis improved, relapse with disabling seizures
8	M/4	3.5	Left	No motor deficit, dysphasia	MP	–	36	<25% reduction in seizures
9	M/8	6	Right → left	Hemiparesis, global impairment	–	Hemispherectomy	24	Bilateral disease, expired
10	F/14	10	Left	Hemiparesis, dysphasia	–	Hemispherotomy	24	Seizure-free, improved language, in special school, on one AED
11	M/22	9	Right	No hempiplegia, tongue EPC, dysarthria	–	Frontal opercular resection	24	Tongue EPC abated, normal speech, employed
12	M/6	3.5	Left	Mild hemiparesis dysphasia	IG	–	24	No change
13	M/15	8	Right	No motor deficit, normal language	MP	–	24	<25% reduction in seizures
14	M/4	3	Right	Mild hemiparesis, normal language	MP	–	18	<50% reduction in seizures
15	M/13	7	Left	Mild hemiparesis, dysphasia	–	–	18	>75% reduction in seizures
16	M/8	6	Right	Mild hemiparesis, normal language	MP	Hemispherotomy	12	Seizure-free, in regular school
17	M/9	7	Right	Mild hemiparesis Normal language	MP	Hemispherotomy	12	Seizure-free, in regular school, on one AED
18	F/18	13	Left	Mild hemiparesis, dysphasia	–	–	–	No follow-up
19	F/2.7	2.3	Left	Hemiparesis, dysphasia	IG + MP	–	3	No change

AED: antiepileptic drug; EPC: epilepsia partialis continua; F: female; IG: intravenous immunoglobulin; M: male; MP: intravenous methyl prednisolone.

Table 4
MRI abnormalities in 19 patients with Rasmussen's encephalitis.

MRI findings	*n* (%)
Insular and perisylvian atrophy	19 (100)
White matter hyperintense signal changes	7 (36.8)
Basal ganglia involvement	18 (94.7)
Caudate atrophy	17 (89.5)
Caudate + putaminal atrophy	15 (78.9)
Caudate + putaminal + globus pallidal atrophy	1 (5.3)
Atrophy of cerebral peduncle and brainstem	11(57.8)
MRI staging at presentation[a]	
Stage 2	1 (5.2)
Stage 3	15 (78.9)
Stage 4	3 (15.7)

[a] MRI staging—see text and Bien et al.[13] for definition.

those with age at the onset of seizures ≤5 years ($n = 8$) versus ≥6 years ($n = 11$), duration from onset to presentation less than ≤2 years ($n = 8$) versus >2 years ($n = 11$), medical therapy versus surgical therapy, and those who underwent surgery within ≤2 years from the onset ($n = 3$) versus >2 years. Among our patients, antecedent events occurred more frequently in younger children compared to those ≥6 years, although the difference did not quite reach statistical significance (5/8 vs. 2/11, p 0.07). While none of the patients in the medical group achieved Engel class I outcome at last follow-up, 9/10 in surgical group did so (p 0.000). At last follow-up, none of the patients in medical group were on AED monotherapy, whereas 5/9 patients in surgical group were receiving only a single AED and one was totally off AED (Table 3) (p 0.000). None of the variables such as age at onset, presence of antecedents, pre-treatment seizure burden, MRI stage, and extent of pre-treatment neurological deficits predicted responsiveness to immunotherapy.

4. Discussion

RE is a rare disease the world over. Our experience with 19 patients seen during 11-year period in a major epilepsy referral center in southern India (1.7 cases per year) agrees with those from similar centers in developed countries.[11] All our patients fulfilled the European Consensus Diagnostic Criteria for RE.[5] The diagnosis was histopathologically verified in 10 of the operated patients. A majority of our patients presented after median delay period from disease onset of nearly 4 years, despite disabling medically refractory seizures. SPS are the commonest seizure type in RE.[1,2,5] In addition, we noted a high frequency of CPS in 84% of our patients, which contrasts with the observation of Oguni et al.,[1] who reported CPS in only 50% of their patients. A higher frequency of CPS in the present series of patients could be due to better seizure characterization by video-EEG monitoring. The presence of chronic EPC is a useful diagnostic feature as it virtually narrows down the differential diagnosis between RE and focal cortical dysplasia, which can be easily distinguished by MRI. However, absence of EPC does not exclude the diagnosis of RE; nearly one-

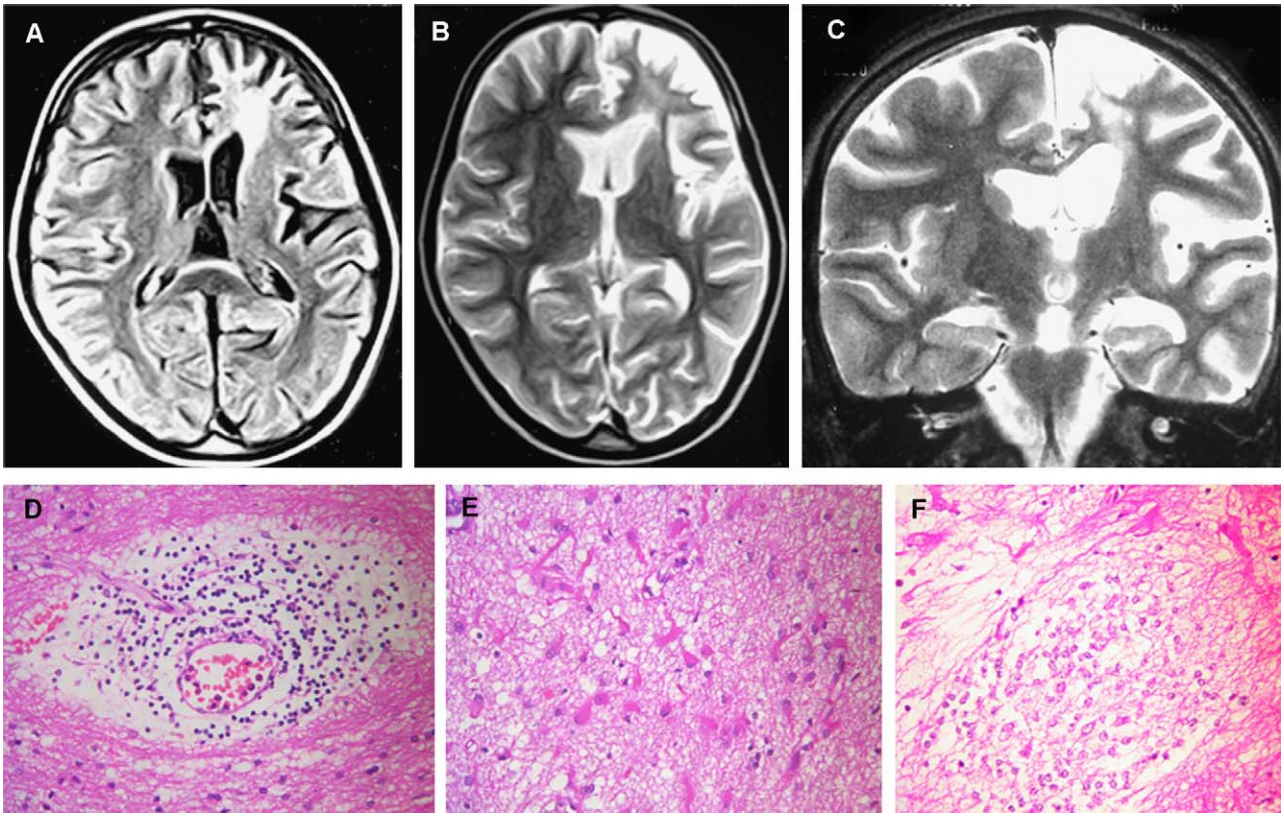

Fig. 1. The MRI and histopathological findings of a right handed 8-year-old girl (Patient 3, Table 3) who presented with 18-month history of epilepsia partialis continua involving right upper and lower extremities. The right hemiparesis was mild and she had nearly normal hand function. The Wada test confirmed language lateralization to the left hemisphere. Axial FLAIR (A) and T2W MR images (B) performed 6 months after onset of illness and coronal T2W sequence (C) 12 months later shows left hemispheric atrophy predominantly involving the insulo-opercular region, underlying white matter hyperintensity, caudate and putaminal atrophy, and enlargement of ipsilateral frontal horn. Because of repeated convulsive status epilepticus requiring hospitalizations unresponsive to several antiepileptic drugs (AEDs) and immunotherapy, she underwent left hemispherectomy despite relatively preserved right upper limb motor functions and left hemispheric speech dominance. Histopathology shows (D) dense perivascular lympho-mononuclear cell infiltration (HE 200×), (E) reactive gemsitocytic proliferation (HE 150×) and (F) microglial nodule (HE 200×). She made a complete recovery from the postoperative aphasia within 3 weeks. When seen recently 5 years after surgery, she is seizure- and AED-free, a fifth grader doing well in school and has adapted well to left handedness because of suboptimal right hand fine motor functions.

fourth of our patients did not have EPC. The frequency of EPC in RE has varied from 56% to 92% in different reports.[1,5,17] One of our patients in the burned out stage of RE had EPC restricted to left side of the tongue, which was abolished by right frontal opercular focal cortical resection.[14] This patient, despite having had the disease for over 15 years, did not exhibit any hemiparesis, as was true for one more of our patients. Severely disabling dysarthria due to lingual EPC prompted this patient to seek a limited focal resective procedure after fully understanding its uncertain long-term benefit. During the last 3-year follow-up, this patient has remained free of lingual EPC and dysarthria. Preservation of motor function in some patients despite long standing disease could possibly be explainable by neuronal plasticity, due to the transfer of motor functions to uninvolved areas of diseased hemisphere or to contralateral normal hemisphere. A similar mechanism may be responsible for the steady improvement in expressive and receptive language abilities we observed following surgery in three of our patients with left hemispheric disease and pre-operative dysphasia.

Bien et al.[3] distinguished two groups of RE patients with marked differences with regard to age at onset, duration of disease and outcome. While their type 1 patients, with age at onset $\leq$6 years, had a rapid progression with disabling seizures and neurological deficits, type 2 patients with onset >6 years had more slow and indolent course. There was a tendency for antecedent events to occur more frequently in our patients with age at onset $\leq$6 years. One of our patients who did not have hemiparesis despite having had EPC for 16 years had age at onset of focal seizures at 9 years. Although RE is essentially a unihemispheric disease, bilateral RE very rarely occurs. Among ~200 patients from the literature analyzed by Bien et al.[5] evidence for bihemispheric involvement was suggested in nine patients. One of our patients, who presented with right hemispheric histopathologically verified RE, developed right focal motor seizures after being seizure-free for nearly 2 years following right hemispherectomy. A computed tomography scan revealed left hemispheric atrophy and white matter hyperdensities. The family did not consent for any further investigation. The patient succumbed to refractory seizures 4 years after the onset of left hemispheric involvement.

Serial MRI showing progressive atrophy of the involved hemisphere, most marked in the insular and periinsular regions and ipsilateral head of the caudate nucleus is a pathgnomonic diagnostic feature of RE.[13,15,17] We observed prominent putaminal involvement, in addition to the caudate involvement in 79% of our patients (Table 3), which we have highlighted in an earlier publication.[15] Bien et al.[13] have staged MRI abnormalities by tracing their progression from normal to hyperintense signals and cortical swelling to progressive cortical atrophy and disappearance of hyperintense signals. The MRI findings in a majority of our patients at presentation corresponded to stage 3 of Bien classification.[13] Curiously, despite high frequency of caudate and putaminal involvement, extrapyramidal features in RE is rare.[5] None of our patients exhibited any extrapyramidal symptoms or signs. A British study identified two out of six patients with RE presenting with hemidystonia,[18] although differentiation of tonic/dystonic EPC from extrapyramidal dystonia can often be difficult.

Surgery (hemispherectomy or hemispherotomy) is the definitive treatment of RE.[2,5,19] In patients presenting early in the course of the disease and in those without disabling hemiplegia are often subjected to immunotherapy with steroids, intravenous immunoglobulin or plasma exchange.[5,9,10] While the response to immunotherapy on seizure burden is often inadequate and short lived, seizure-freedom rates following surgery from 63% to 85% have been reported.[5] All expect one of our patients achieved Engel class 1 outcome following surgery, while only one of 11 patients who received immunotherapy had sustained seizure-freedom for >2 years. None of the factors we analyzed, such as age at onset, age at presentation, presence/absence of antecedents, seizure burden, MRI stage, predicted responsiveness to immunotherapy. One may have to resort to surgical intervention even in those patients with little disabling neurological deficits, if seizures are life threatening, as happened in one of our patients illustrated through Fig. 1. Although focal cortical resection has very little role in a progressive unihemispheric disease like RE, it may be an option in selected patients who manifests with EPC involving a restricted region in the burned out stage of the disease, as exemplified by our already reported patient with lingual EPC.[14]

In summary, data from this series of patients from a developing country reiterates the well known clinical, electrophysiological, and radiological features of RE as well as the outcome following immunotherapy and surgery. In addition, we observed the following unusual features: isolated lingual EPC abolished by focal cortical resection, development of contralateral hemispheric disease following successful hemispherectomy, absence of hemiparesis despite long standing disease, and MRI evidence for high frequency of putaminal atrophy, in addition to the caudate head atrophy.

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